201-15601

NCIC OPPT
Sent by: Anh Nguyen

09/22/2004 08:06 AM

To: NCIC HPV@EPA
cc:
Subject: Re: Thioesters: EPA comments on theThiodipropionitrile HPV Challenge submission--Sponsor's Response

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US Environmental Protection Agency
Office of Pollution Prevention and Toxics Docket
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09/21/2004 11:25 AM

To: NCIC OPPT@EPA, Rtk Chem@EPA, Donald Rodier/DC/USEPA/US@EPA, Amy Benson/DC/USEPA/US@EPA
cc:
Subject: Thioesters: EPA comments on theThiodipropionitrile HPV Challenge submission--Sponsor's Response

Attached is the Thioesters Association's response to EPA comments on Thiodipropionitrile (CAS 111-97-7).

If you have any questions, please contact me.

Elizabeth Hunt
Executive Director

-----Original Message-----
From: Hefter.Richard@epamail.epa.gov
[mailto:Hefter.Richard@epamail.epa.gov]
Sent: Tuesday, June 22, 2004 4:51 PM
To: ehunt@adelphia.net
Cc: Northrop.Ralph@epamail.epa.gov
Subject: EPA comments on theThiodipropionitrile HPV Challenge submission

Dear Ms. Hunt:

Attached please find EPA's comments on the Thiodipropionitrile submission to the Chemical RTK Challenge Program and a transmittal letter from Dr. Oscar Hernandez, Director of OPPT's Risk Assessment Division. These items will also be sent to you in hard copy and are expected to be posted on the Chemical RTK website in a few days.

(See attached file: SN271 TDPN EPA Comments 062204.wpd)(See attached file: SN#271 Letter.wpd)

SN271 TDPN EPA Commentswithresponse.doc

EPA Comments on Chemical RTK HPV Challenge Submission:
Thiodipropionitrile

SUMMARY OF EPA COMMENTS (with response from Sponsor)

The sponsor, the Thioesters Association, submitted a test plan and robust summaries to EPA for Thiodipropionitrile (TDPN, CAS No. 111-97-7) dated December 16, 2003. EPA posted the submission on the ChemRTK HPV Challenge Website on January 23, 2004.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The submitted data are adequate for the purposes of the HPV Challenge Program.

2. Environmental Fate. EPA agrees that ready biodegradation data are needed.

3. Health Effects. EPA agrees with the submitter's proposal for conducting mutagenicity and chromosomal aberrations assays to address genetic toxicity endpoints. The submitter's proposal for reduced health effects testing based on a closed-system intermediate claim is not adequately supported (see below). Therefore, data gaps exist for the repeated-dose, reproductive, and developmental toxicity endpoints.

4. Ecological Effects. Only ECOSAR values for acute toxicity to fish, invertebrates and algae were provided. The submitter needs to provide adequate measured data for these endpoints on an adequate analog in order to use predicted values for these endpoints.

Response: Eastman and Solutia filed an HPV test plan for the alkyl nitriles which included proprionitrile, butyronitrile and isobutyronitrile (http://www.epa.gov/chemrtk/alkyntrl/c14860tp.pdf). Since proprionitrile is most similar to TDPN, only data for it is supplied here. Using the ECOSAR neutral organics model, the LC50/EC50 values for TDPN and proprionitrile compared with measured data found in the alkyl nitriles test plan are as follows:

Species	TDPN Predicted	Proprionitrile Predicted	Proprionitrile Measured
Fish LC50	8785 mg/L	1452	96 hr fathead minnow (flow through with analytical) = 1520 mg/L 96 hr rainbow trout (static nominal only) = 340 mg/L 96 hr bluegill sunfish (static nominal only) = 41 mg/L (Note dissolved oxygen concentration ranged from 2.0 – 4.3 after 96 hours. Less than acceptable values)
Daphnia EC50	8171 mg/L	1388	48 hr Daphnia magna (static nominal only) 250 mg/L
Algae EC50	4540 mg/L	789 mg/L	N.D.

N.D. Based on measured data for butyronitrile and isobutyronitrile, the EC50 for proprionitrile is expected to be >87.8 mg/L and may be much higher.

For proprionitrile, with the exception of the bluegill, all predicted values are within 10x of the measured value. In the bluegill study, dissolved oxygen levels decreased from 0 to 96 hours with the dissolved oxygen levels ranging from 2.0-4.3 at the end of the study. According to the proprionitrile dossier, the lowest dissolved oxygen concentration was observed in water with the highest concentration of proprionitrile. The low dissolved oxygen values are obvious confounders to the bluegill data. The remaining studies for proprionitrile lend support that the ECOSAR predictions for TDPN should be close to the measured values for TDPN. If the measured TDPN values are within 10% of the predicted values, the value for the most sensitive species, algae would still be >450 mg/L. This is four times greater than 100 mg/L, a concentration considered essentially non-toxic. Considering the low amounts present in waste water discharged from the plant as discussed below, the limited production facilities in the US, and the low level of concern based on the ECOSAR prediction, conducting aquatic toxicity studies of this material appear to be unnecessary.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE THIODIPROPIONITRILE CHALLENGE SUBMISSION

General

EPA disagrees with the submitter's claim (Appendix 1 of the submission) that the sponsored chemical is a closed-system intermediate and thus eligible for the reduced testing rationale in the U.S. HPV Challenge Program. EPA's conclusion is based on the following reasons:

(1) The test plan does not provide monitoring data for any medium. The test plan mentions that waste aqueous layers containing "minimal concentrations" of TDPN are sent to on-site process wastewater treatment facilities. The test plan does not indicate if periodic sampling of the wastewater for TDPN occurs, either before or after treatment. In order to meet the information requirements for a closed system intermediate, the submitter needs to provide monitoring data, including the limits of detection, showing that TDPN is not detected in any medium following treatment or if monitoring data are not available, a statement that no monitoring has taken place and the basis for believing, in the absence of data, that the chemical has not been released and that exposure does not occur. Although, according to the test plan, no industrial hygiene monitoring data are available for TDPN at either site where it is manufactured and consumed, the test plan asserts that any worker exposure would be "infrequent and at a very low level" because of the limited volatility of TDPN and precautions taken to comply with OSHA regulations pertaining to a more volatile precursor chemical (29 CFR 1910.1045). However, no exposure limits for TDPN were identified.

(2) The test plan does not provide any data on the occurrence of unreacted TDPN in the chemicals produced from this intermediate. The test plan states that TDPN "is not present appreciably in any downstream product" but does not provide any basis for this assertion.

Response: As mentioned in the appendix to the test plan, aqueous sodium sulfhydrate is reacted with pure acrylonitrile in a closed system. During the reaction, no additional water is added to the reactor. The subsequent product, TDPN, is in the organic phase while the salt remains in the aqueous phase. The aqueous phase is decanted and an additional wash of the organic phase may be conducted. Both aqueous solutions are sent to the waste water treatment plant. Since submission of the test plan, analysis of the water streams from

5+ batches of TDPN have resulted in 0.10-2.52% TDPN present in the water streams. Due to the relatively small amount of water used in the reaction process, the total amount of TDPN sent to the waste water treatment plant is as concentrated as practical but still relatively low. The waste water streams from products derived from TDPN were analyzed, also, and found to have not detectable (<2ppm) to 80 ppm TDPN. The TDPN waste streams are subsequently diluted at least a 100-fold resulting in a maximum estimated concentration of 25 ppm in the waste water treatment plant. The amount of TDPN in the water exiting the waste water treatment plant is below the detection limit of 2 ppm. The solid waste residue from the production operations and treatment plant had not detectable amounts of TDPN (<2ppm).

There are no exposure limits for TDPN since a saturated vapor concentration at 25°C is <0.1 ppm. Since the reaction vessel is maintained at temperatures slightly above ambient, one would not expect a release to generate a condensation aerosol. Should any TDPN escape along with acrylonitrile from the production facility, the protective equipment the worker would wear for acrylonitrile will preclude exposure to TDPN also.

Analysis of downstream products made from TDPN, revealed less than 0.1% TDPN (the level of detection) in four different lots. In another analysis of three downstream products with greater analytical sensitivity, there was no TDPN at a detection level of 5 ppm. Products derived from TDPN are not marketed to consumers as produced but are part of formulations. Thus the concentrations of TDPN that would be expected in the final products are much, much lower.

Given the low concentration of TDPN present in the waste stream leaving the two plants, the non-volatile nature of TDPN and the protective equipment necessary due to the presence of acrylonitrile in the plant and the low levels of TDPN found in downstream products, no repeated dose, developmental or reproductive toxicity studies are proposed. In addition, the modelled aquatic toxicity values are considered acceptable, given the amount of TDPN released from the waste water treatment plant is below the detection limit of 2 ppm.

Test Plan

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The submitted data for these endpoints are adequate for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The submitted data for photodegradation, stability in water, and fugacity are adequate for the purposes of the HPV Challenge Program.

Biodegradation. EPA agrees with the submitter's proposal for conducting a biodegradation test, which should follow OECD TG 301 for ready biodegradation.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

The submitted data on acute toxicity are adequate for the purposes of the U.S. HPV Challenge program. EPA agrees with the submitter's proposal for conducting mutagenicity and chromosomal aberrations assays to address genetic toxicity endpoints. The submitter's proposal for reduced health effects testing based on a closed-system intermediate claim is not adequately supported. Therefore, data gaps exist for the repeated-dose, reproductive, and developmental toxicity endpoints (even if the closed-system intermediate

claim was met, a developmental toxicity test would be needed) and can be addressed by conducting a repeated-dose/reproduction/developmental toxicity screening test (OECD TG 422).

Repeated dose toxicity. The submitted summary for a rat 32-day oral feeding study (from 1953) has several deficiencies and the submitter has assigned a reliability code of 4. A combined screening test (OECD TG 422) will address the endpoint.
Response: Addressed above.

Ecological Effects (fish, invertebrates, and algae)

The test plan states that testing of TDPN is unnecessary because the environmental concentrations are less than toxic levels estimated by ECOSAR. This rationale does not reflect HPV Challenge program guidance. To adequately address these endpoints, the submitter needs to provide either measured data on the subject chemical or measured data for these endpoints on an adequate analog to support the ECOSAR data (see guidance at (http://www.epa.gov/chemrtk/sarfinl1.htm).

Response: Addressed above.

Followup Activity

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.